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New Techniques

Bedside Quantification of Atherosclerosis Severity for Cardiovascular Risk Stratification: A Prospective Cohort Study

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OBJECTIVES We sought to assess the ability of a new noninvasive method to quantify atherosclerosis severity and to examine its power to predict cardiovascular events.

BACKGROUND Drug prevention of cardiovascular events is effective but costly, leading to a debate about who should receive this treatment. Patient selection is often based on surrogate markers, but quantification of atherosclerosis severity is desirable.

METHODS Atherosclerosis severity was quantified by determination of specific aortic wall elastance in transthoracic echocardiography, applying the biomechanics of pulse wave propagation. After validating the method in 52 patients by measuring aortic plaque burden in transesophageal echo directly, another 336 patients were prospectively studied by monitoring atherosclerotic events at one year and comparing the results with conventional risk stratification.

RESULTS Specific aortic elastance was well correlated with plaque burden ($p < 0.0001$) and largely independent of confounding variables. Specific aortic elastance predicted the primary end point of "atherosclerotic death, myocardial infarction or stroke" at one year ($p < 0.0002$). Event rate at one year in the lowest specific elastance tertile was 1.8% (CI 0.0% to 4.3%), in the middle tertile 5.4% (CI 1.1% to 9.7%) and in the highest tertile 12.7% (CI 6.3% to 19%). Secondary end points supported these findings. Stepwise multivariate analysis identified specific aortic elastance, prior atherosclerotic events and left ventricular ejection fraction as independent risk predictors. Specific elastance was of incremental value to clinically identified variables.

CONCLUSIONS Bedside measurement of specific aortic elastance allows assessment of atherosclerosis severity. It predicts the risk for future atherosclerotic events beyond conventional risk factors, promising better targeting of pharmacologic prevention and improved cost effectiveness. (J Am Coll Cardiol 2002;39:702–9) © 2002 by the American College of Cardiology

With cardiovascular diseases as the leading cause of death in the Western world, prevention of atherosclerosis and its complications is a major goal of healthcare. The introduction of powerful lipid-lowering drugs has brought unprecedented mortality reductions in secondary (1) and primary prevention (2). However, in an era of cost awareness and limited resources, this has also led to a debate about who should be treated. Individuals are often selected using surrogate markers of atherosclerosis, such as prior cardiovascular events, number of risk factors and lipids levels. This allows identification of the subjects at highest risk, but for the large population at moderate risk, better strategies are needed.

We hypothesized that quantification of atherosclerosis severity might improve risk stratification compared with that provided by conventional risk factor assessment (Fig. 1). To quantify atherosclerosis severity noninvasively, we developed a novel echocardiographic bedside method, which determines aortic elastic properties based on the biomechanics of pulse wave-vessel wall interaction. The aim of the study was: 1) to validate this method by direct visualization of plaque burden in transesophageal echocardiography (TEE), and 2) to determine the value of the method for risk stratification versus use of conventional risk factors, prospectively in a large patient cohort.

METHODS

Rationale. Atherosclerosis leads to thickening and stiffening of the arterial wall through fibrosis, calcification, plaque formation and smooth muscle cell proliferation. In biomechanical terms, this implies changes of material properties of the artery (increase in Young's elastic modulus E), and an increased wall thickness (h). The Moens-Korteweg equa-

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Abbreviations and Acronyms

CI = confidence interval
HDL = high density lipoproteins
SD = standard deviation
TEE = transesophageal echocardiography
TTE = transthoracic echocardiography

tion (3), describing wave propagation in elastic tubes filled with inviscid fluid

$$c^2 = \frac{Eh}{\rho_f D}$$ with c: wave propagation velocity

E: Young's modulus (circumferential)
h: wall thickness
ρ_f: fluid density
D: vessel diameter

can be rearranged to obtain

$$E \times h = c^2 \rho_f D$$

In other words, the product of E and h, the key parameters influenced by atherosclerosis, can be determined by measuring wave front velocity, fluid density and vessel diameter (although E and h are difficult to measure individually). The product E×h is termed "specific elastance" throughout this article. Blood density can be considered constant (4). Wave front velocity and vessel diameter are measurable by ultrasound, as shown in Figure 2.

Study design. Two independent consecutive patient cohorts were prospectively studied. Measurements were performed during diagnostic transesophageal (TEE; validation part) and transthoracic (TTE; risk stratification part) echocardiography, and results were compared to aortic plaque burden, conventional risk factors and cardiovascular events. The validation part included 52 consecutive patients referred for TEE. The risk stratification part included 336 consecutive patients referred for TTE. There were no exclusion criteria.

Determination of specific elastance. Echo/Doppler measurements (Fig. 2) were performed with a Sonos 5500 echocardiograph (Hewlett Packard, Andover, Massachusetts), the S4 transthoracic probe and the 5.0/3.7 MHz transesophageal probe, with readers blinded for plaque burden and outcome, respectively.

Pulsed-wave Doppler recordings were acquired from the left ventricular outflow tract and the left common femoral artery in the groin. Wave front arrival at each location was defined by extrapolation of the ascending Doppler flow profile to the baseline, using the electrocardiographic R wave as time reference. Mean aortic diameter was determined by TTE from measurements 1 cm above the sinotubular junction (parasternal window, feasibility 99%), at the origin of the left subclavian artery (suprasternal window, feasibility 98%) and at the diaphragm (substernal window, feasibility 98%). Wave front velocity was calculated as wave front delay (outflow tract to femoral artery) divided by aortic length. The latter was determined as follows: aortic length = 0.41 m/m body length, a formula derived from catheter-based measurements during coronary angiography in 22 patients (mean 0.41 m/m, SD 0.024 m/m). Wave front velocity, mean aortic radius determined by TTE and blood density (4) (1,060 kg/m^3) were substituted to calculate specific aortic elastance. Using SI units (meter, seconds) scaled by 10^{-3}, result units are kiloNewton/meter (kN/m). Repeatability (one observer, repeated data acquisition), intraobserver variability (repeated measurement in the same images) and interobserver variability were determined in groups of 20 patients.

Aortic plaque burden. By TEE, short axis slices were acquired in the ascending aorta at the pulmonary artery crossing, at the origin of the left subclavian artery and in the

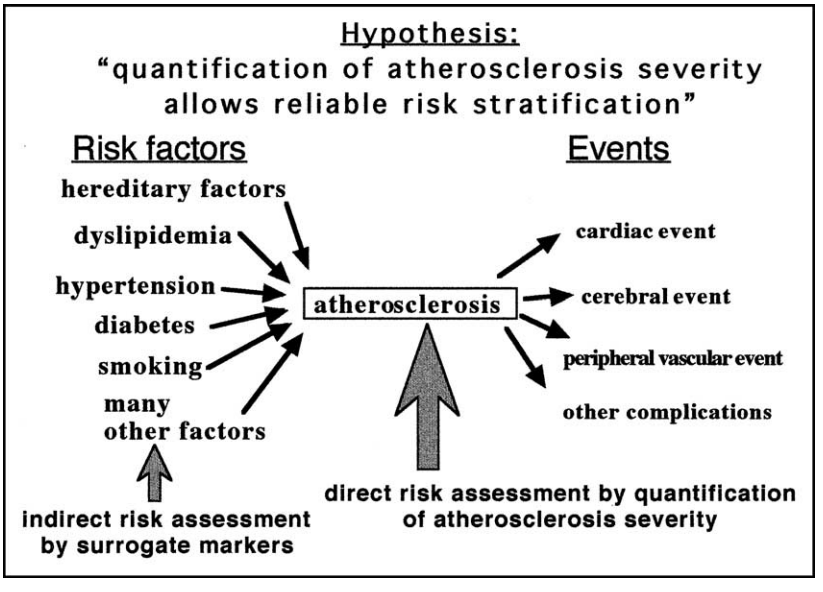

Figure 1. Rationale of study.

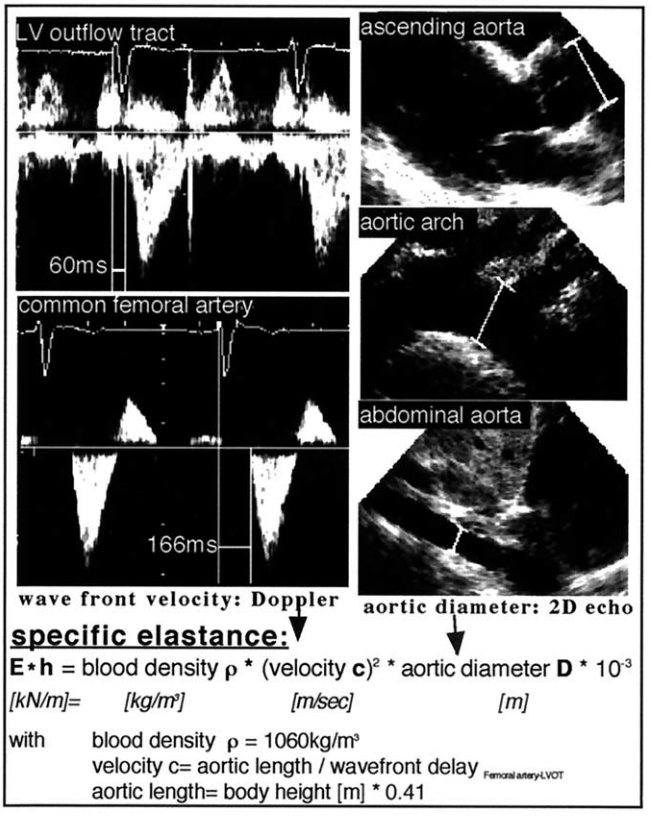

Figure 2. Method for determination of specific aortic elastance by transthoracic echocardiography: Wave front propagation time from the left ventricular outflow tract to the common femoral artery is measured using pulsed wave Doppler. The wave front is defined as the extrapolation of the first segment of the Doppler flow profile to the baseline. Average aortic diameter is determined from measurements in the ascending aorta, the aortic arch and the abdominal aorta. All measurements are made using a conventional echocardiograph.

descending aorta just distal to the arch, at its lowest visible portion, and halfway between. Maximum plaque thickness and extent (circumferential arc) were determined in each slice. Average plaque thickness and extent were calculated as mean of the five measurements. Plaque burden in milliliters was calculated as average plaque thickness times average plaque arc length times aortic length.

Aortic compliance and distensibility (conventional methods). By TEE, the aortic diameter change with the cardiac cycle (mean of five locations) was measured, and pulse pressure was determined by brachial sphygmomanometry. Aortic compliance was calculated as area change divided by pulse pressure (method A) (5), and aortic distensibility was calculated as fractional area change divided by pulse pressure (6). Alternatively, aortic compliance was determined from wave front velocity and blood pressure (method B) (7).

Risk factors, prior events, revascularizations. Cardiovascular risk factors, prior history of ischemic events and revascularization procedures were assessed by patient interviews, patient records and blood lipid determinations. A positive family history was defined as myocardial infarction, revascularization or cerebrovascular events before the age of 65 years. Hypercholesterolemia was defined as untreated total cholesterol >6.5 mmol/l or total cholesterol 5.2 to 6.5 mmol/l, with total cholesterol to HDL ratio >5.

Outcome. Follow-up at one year was done by telephone interview of patients and referring physicians, with hospital chart review in case of events. Atherosclerotic events were defined as stroke, myocardial infarction and interventional or surgical revascularization of coronary, cranial, abdominal or peripheral arteries, counting only one event per patient for composite outcome variables. Nonatherosclerotic death was defined as cancer death, death in a patient with another life-threatening nonatherosclerotic disease and violent death. Atherosclerotic death was defined as death occurring with acute coronary syndromes, stroke or unexpected death in patients with documented coronary artery or cerebrovascular disease but without life-threatening nonatherosclerotic disease. The predefined primary end point was a composite of atherosclerotic death, myocardial infarction or stroke at one year. Secondary end points were overall and atherosclerotic death, nonfatal infarction, stroke, revascularization procedures and combinations thereof.

For calculation of relative risk and to determine the presence of an incremental relation of atherosclerosis severity and event risk, tertiles of specific aortic elastance and different levels of other risk predictors were also analyzed. To yield an age-corrected measure of specific aortic elastance, analyses were also performed after dividing the cohort into three age strata and classifying patients in each stratum into three tertiles of specific aortic elastance.

Statistics. Statistics were done using StatView Software 5.01 (Abacus Inc., Berkeley, California). Data are described as mean, 95% confidence interval (CI), standard deviation (SD), median and interquartile width according to data distribution and use. Because of skew distribution, specific elastance and plaque burden were log transformed for analysis. Fisher's exact test, *t* tests and regression analysis were used. Linear regression was used for the validation part (univariate comparison of plaque burden with parameters of arterial mechanics, univariate and multivariate analysis of potential confounding factors for specific elastance).

In the risk stratification part, event risk was calculated for tertiles of different predictors of cardiovascular events. Logistic regression was used with the primary end point as dependent variable. In an exploratory analysis, a multivariate logistic model, initially including those factors that were significant in univariate analysis, was used, with stepwise elimination of variables not significant in the likelihood ratio test. To examine the incremental value of specific elastance, the likelihood ratio test was also applied to a model including only clinically identifiable variables with and without specific elastance.

RESULTS

Validation part. Fifty-two patients were studied. Mean age was 57 (SD: 17; range: 27 to 83) years. Thirty (58%) were men. By TTE, mean aortic diameter was 2.4 cm (SD:

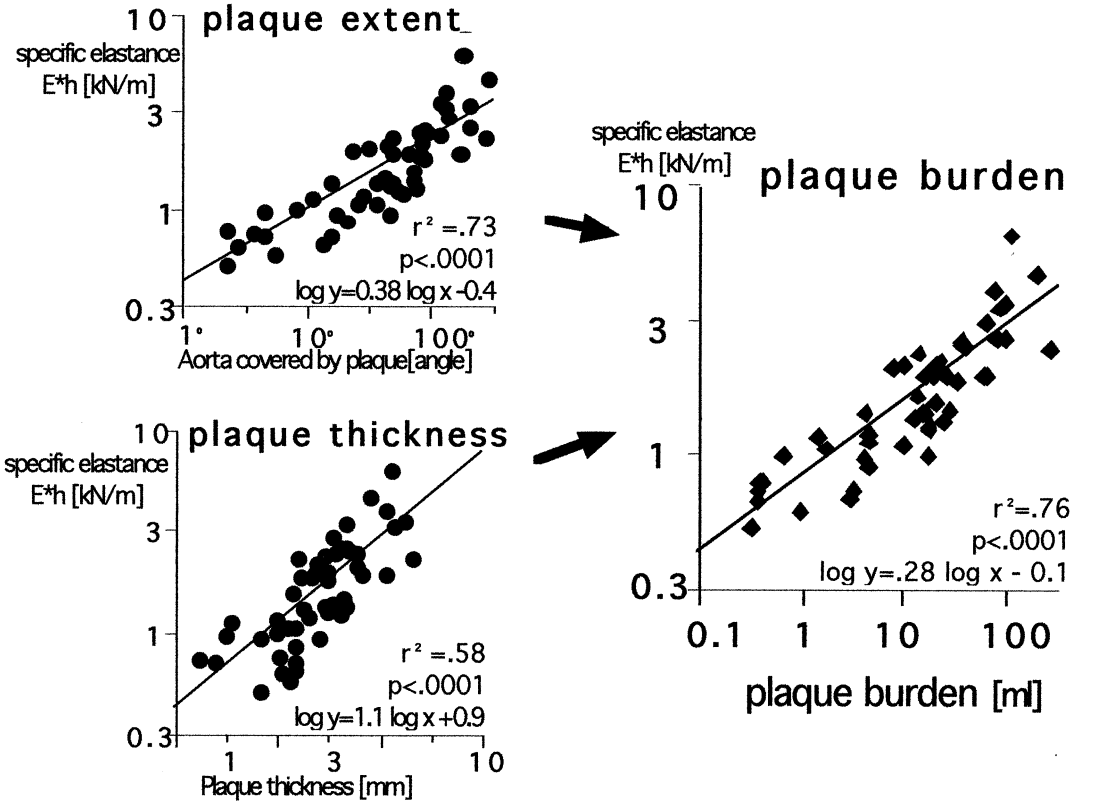

Figure 3. Validation of the new bedside method for quantification of the severity of atherosclerosis by determination of elastic properties of the aortic wall. Specific elastance of the aorta shows an excellent correlation with plaque extent **(left upper panel)**, with plaque thickness **(left lower panel)** and thus with overall atherosclerotic plaque burden **(right panel)**, determined by direct visualization in transesophageal echo.

0.3 cm) and mean wavefront delay was 90 ms (SD: 24 ms). By TEE, median plaque burden was 16 ml (interquartile width: 33 ml; range: 0.3 to 244 ml), mean aortic diameter was 2.4 cm (SD: 0.4 cm) and mean aortic diameter change was 1.3 mm (SD: 0.5 mm).

Median specific aortic elastance was 1.6 kN/m (interquartile width: 1.4; range: 0.5 to 6.7 kN/m). Repeatability was 9.1%, intraobserver variability was 4.9% and interobserver variability was 9.0% of the measured range.

An excellent correlation of noninvasively measured specific elastance by TTE with plaque burden visible in TEE was found (Fig. 3). Uni- and multi-variate analysis of the potential confounding factors of age, blood pressure and aortic diameter documented the robustness of specific elastance as a measure of plaque burden (Table 1). While associated with a stiffer vessel in univariate analysis, these factors did not significantly contribute to specific aortic elastance independent from plaque burden in multivariate analysis. The merits of the new method for determination of plaque burden was then compared to wave front velocity, aortic compliance, aortic distensibility and pulse pressure (Table 2); specific elastance proved to be the best parameter of atherosclerosis severity.

Risk stratification part. In this cohort, 336 patients with a mean age of 63 (SD: 15; range: 11 to 92) years were included. Of these, 206 (61%) were men. Mean serum cholesterol was 5.3 (SD: 1.2) mmol/l, mean HDL cholesterol was 1.3 (SD: 0.41) mmol/l and mean LDL cholesterol

Table 1. Robustness of the Correlation of Plaque Burden and Specific Aortic Elastance Against Potential Confounding Variables

	Determinants of Specific Aortic Elastance					
	Univariate Analysis			Multivariate Model		
	Adjusted R^2	Regression Coefficient (CI)	p Value	Adjusted R^2	Regression Coefficient (CI)	p Value
Aortic plaque burden	0.75	0.28 (0.25–0.33)	< 0.0001		0.28 (0.18–0.38)	< 0.0001
Potential confounding variables						
Age	0.58	0.011 (0.009–0.014)	< 0.0001		0.002 (−0.001–0.006)	0.2
Systolic blood pressure	0.24	0.006 (0.003–0.009)	0.0003		0 (−0.002–0.002)	0.93
Mean aortic diameter	0.13	0.31 (0.09–0.51)	0.006		−0.09 (−0.25–0.7)	0.25
Entire model				0.76		< 0.0001

Table 2. Comparison of Different Parameters of Arterial Mechanics a Measures of Aortic Plaque Burden

Method	R^2	Regression Coefficient (CI)	p Value
Specific elastance	0.76	2.7 (2.2–3.1)	< 0.0001
Wave front velocity	0.59	0.25 (0.19–0.31)	< 0.0001
Distensibility	0.48	65 (86–44)	< 0.0001
Compliance (method A*)	0.23	21 (9.5–34)	0.001
Compliance (method B*)	0.69	1.04 (−1.24–−0.84)	< 0.0001
Pulse pressure	0.31	0.25 (0.13–0.36)	< 0.0001

Simple regression analysis. *See methods section.

was 3.3 (SD: 1.0) mmol/l. Two hundred and three patients fulfilled the criteria for hypercholesterolemia. There were 87 smokers, 61 patients with a positive family history of cardiovascular events and 49 diabetic patients. Mean left ventricular ejection fraction was 54 (SD: 14)% and was below 50% in 22% of patients. There was a history of prior myocardial infarction in 62, of stroke in 32 and of arterial revascularization procedures in 44 patients.

Median specific aortic elastance was 1.8 kN/m (interquartile width: 1.5; range: 0.2 to 23 kN/m). Stratification in three tertiles showed mean specific elastance values of 1.1, 1.8 and 4.5 kN/m, respectively.

In univariate analysis, an increase in specific elastance was associated with hypercholesterolemia ($p = 0.018$), hypertension ($p = 0.0006$), diabetes ($p = 0.0011$) and increasing age ($p < 0.0001$), but not significantly with gender ($p = 0.76$), positive family history of cardiovascular events ($p = 0.37$), smoking ($p = 0.10$) or left ventricular ejection fraction ($p = 0.26$). The relation between age, the number of risk factors and specific aortic elastance is shown in Figure 4, documenting that in a cohort with a moderate number of risk factors (Fig. 4A), specific aortic elastance values span a wide range (Fig. 4B). Specific elastance does not simply reflect age (Fig. 4E) or the number of risk factors (Fig. 4F).

A history of prior cardiovascular events was also associated with higher specific aortic elastance ($p = 0.001$); this was true for myocardial infarction ($p < 0.05$) and stroke ($p < 0.01$).

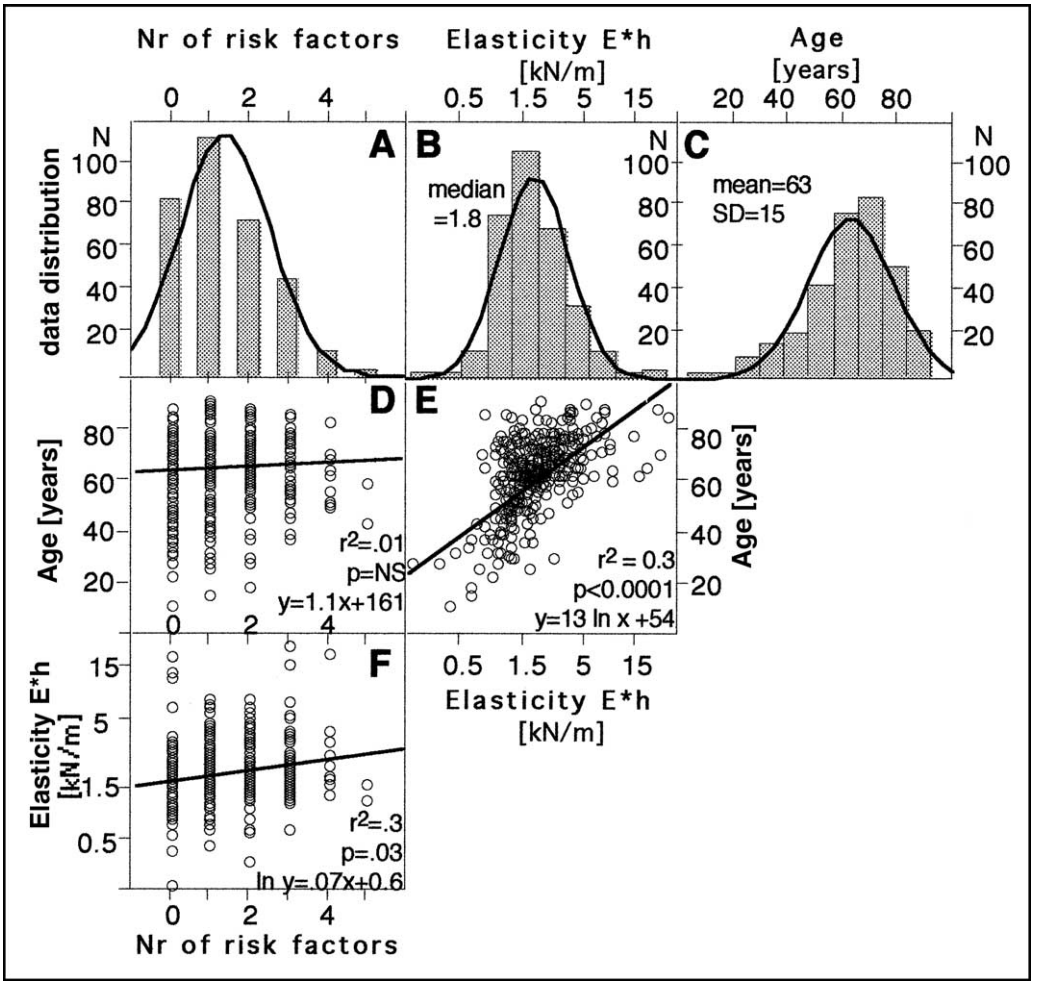

Figure 4. The relation of age, cardiovascular risk factors and specific aortic elastance. In a cohort with a moderate number of risk factors **(A)** and with the age distribution given in **C** that reflects the referral pattern for cardiologic examination, specific aortic elastance spans a wide range **(B)**. Specific elastance does not simply reflect age **(E)** or the number of risk factors **(D)**.

Outcome. Follow-up at one year could be ascertained in 99.7% of patients, with one patient lost to follow-up because of emigration to another continent. At follow-up, 21 patients had died. Death was due to nonatherosclerotic disease in nine patients: malignant tumors in seven, dilated cardiomyopathy with nonstenosed coronary arteries in one and pulmonary embolism in one. There were no violent deaths. Death was attributable to atherosclerosis in 12 patients. Nonfatal infarction occurred in five patients, stroke in seven. Revascularization had been performed by coronary angioplasty in 8, by aortocoronary bypass operation in 10 and by carotid interventions in 3 patients. The composite primary end point was reached in 22 patients. Hospitalization for any cause had taken place in 116 patients.

Specific aortic elastance was strongly associated with subsequent occurrence of the primary end point (atherosclerotic death, myocardial infarction or stroke at one year; $p = 0.0002$). Median specific aortic elastance in patients with a primary end point was 2.5 kN/m (interquartile width: 1.6), but in the other patients it was only 1.7 kN/m (interquartile width: 1.5). The event rate for the primary end point in the lowest tertile (<1.43 kN/m) of specific elastance was 1.8% (CI 0.0% to 4.3%), in the middle tertile 5.4% (CI 1.1% to 9.7%), but in the highest tertile of specific elastance (<2.33 kN/m) 12.7% (CI 6.3% to 19%). Relative risk for various levels of several risk factors is given in Figure 5.

Specific aortic elastance also predicted the secondary end point "atherosclerotic death" ($p < 0.002$), while the number of nonfatal strokes ($n = 7$) and nonfatal myocardial infarctions ($n = 5$) was insufficient for analysis. The combined secondary end points "all death, myocardial infarction, stroke" ($p = 0.02$) and "nonfatal myocardial infarction or stroke" ($p = 0.03$) were likewise predicted by aortic specific elastance. No significantly increased revascularization rate in patients with higher specific aortic elastance was observed ($p = 0.8$).

Age-corrected specific elastance likewise predicted the primary end point ($p = 0.007$) and the secondary combined end point "nonfatal infarction or stroke" ($p = 0.03$). There was no association of specific aortic elastance with nonatherosclerotic death or with hospitalization for any cause. Other univariate predictors of the primary end point were age ($p < 0.001$), prior atherosclerotic events ($p < 0.02$), left ventricular ejection fraction ($p = 0.01$) and positive family history ($p = 0.04$). Significance for the primary end point was not reached by "number of cardiovascular risk factors" ($p = 0.11$) or by the Framingham risk model (8) ($p = 0.34$); the latter predicted the composite secondary end point "all death, infarction, stroke or revascularization" ($p < 0.03$). Nonsignificant trends for an increased risk for the primary end point were also seen for increased plasma cholesterol, low HDL cholesterol, smoking, diabetes and left ventricular hypertrophy (as determined by echocardiography). The relative risk for the primary end point of several levels of multiple risk factors is shown in Figure 5.

In stepwise logistic regression, the following independent

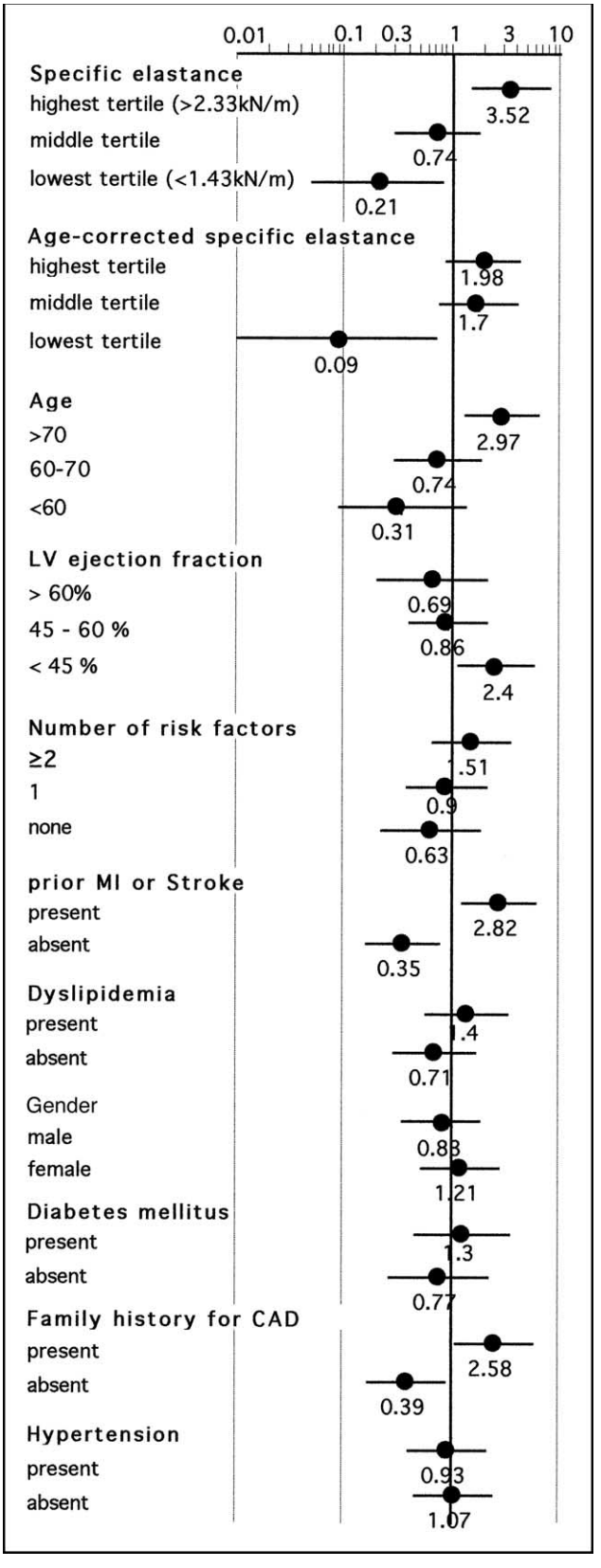

Figure 5. Relative risk for the primary end point (death attributable to atherosclerosis, nonfatal myocardial infarction or stroke) of different levels of multiple risk factors. An increase in specific elastance leads to a marked increase in event risk for each tertile of specific elastance. CAD = coronary artery disease; LV = left ventricular; MI = myocardial infarction.

predictors of the primary end point emerged: specific elastance ($p = 0.009$), prior events ($p = 0.03$) and, of borderline significance, left ventricular ejection fraction ($p = 0.053$), while age, gender and number of risk factors were not independently predictive. In the model including only clinically identified variables and specific elastance, the latter was incrementally significant ($p < 0.05$).

DISCUSSION

In this study, bedside quantification of atherosclerosis severity by determination of specific aortic elastance was shown to strongly reflect atheromatous plaque burden in the aorta measured by direct visualization. This parameter strongly and independently predicted cardiovascular event risk in a prospective cohort of individuals referred for cardiologic evaluation for any reason.

Pathologists have long observed that widespread atherosclerotic vascular changes usually precede clinical manifestations of atherosclerosis by many years. The results of this study document the feasibility of quantifying the severity of atherosclerosis noninvasively at the bedside as part of an examination that is often already being performed, using technology currently available to the cardiologist. The findings further confirm the working hypothesis that noninvasive quantification of atherosclerosis severity might be as promising for risk prediction as are classical "risk factors."

The echo method used for quantification, which is based on the biomechanics of pulse wave propagation, was robust to possible confounding factors in the range studied and compared favorably with previously described parameters of pulse wave-aortic wall interaction.

Biomechanical considerations. Atherosclerosis is anatomically defined as thickening and stiffening of the arterial wall through fibrosis, calcification and plaque formation with smooth muscle cell proliferation of intimal and/or medial layers (9). A method to quantify atherosclerosis severity would, therefore, preferably be sensitive to both, an increased wall thickness (h), and changes in elastic tissue properties (Young's modulus E). Vessel stiffening resulting from these pathologic alterations induces changes in pulse wave propagation. Bifurcations and wave reflections make complete mathematical modeling of pulse wave propagation difficult, but when only the wave front is considered, which is unaltered by reflections, the Moens-Korteweg equation describing wave propagation in elastic tubes can be exploited. It predicts that the product of Young's modulus and wall thickness ($E \times h$), here termed specific elastance, is determined by wave front velocity, vessel diameter and blood density. More complicated, nonlinear equations have been thoroughly studied in vitro (10) but may be too complex and not needed clinically, as the pressure-dependent change in elastic properties is only moderate at physiologic blood pressures (11,12). Aortic elastic properties have been determined from human autopsy material (13), and average specific elastance calculated from those data was 1.4 kN/m and 2.2 kN/m for thoracic and abdominal aorta, with a 10-fold increase with atherosclerosis, thus showing an excellent agreement with our findings.

Prior studies. These findings extend prior approaches studying pulse wave-vessel wall interactions: aortic compliance (5,7,14,15), distensibility (6), pulse pressure (16) and pulse wave velocity (17). Compared to these, specific elastance as measured in the present study appears better justified as a measure of atherosclerosis from a biomechanical standpoint and was better correlated with atherosclerosis severity in the current study. By focusing on incomplete biomechanical models or on indirect parameters of mechanical wall properties, these other methods might be sensitive to confounders: e.g., pulse wave velocity (18) does not control for vessel diameter; distensibility and compliance measurements suffer from the inaccessibility of the aorta for pressure measurement. In addition, studies validating other methods by determination of arteriosclerotic burden are lacking, and prospective data about the value for risk stratification in individuals are limited (19,20).

Study limitations. It might be argued that atherosclerosis severity in the aorta does not equal organ-specific vascular changes (e.g., coronary atherosclerosis, due to uneven distribution of this process in different vascular territories). Although this is correct when organ-specific invasive diagnostic procedures such as coronary angiography are considered, less organ-specific screening methods such as the one described might even be advantageous for institution of preventive measures with known benefit in multiple arterial territories (like lipid lowering). The inclusion criterion (referral to an echocardiogram for any reason) represents patient selection, allowing application of our results only to specific settings with similar patient populations. To confirm applicability and value of the method to the population at large, population-based studies will be needed. Large outcome studies are also needed for exhaustive multivariate characterization of additional factors relevant for outcome and for definitive head-to-head comparison of different methods, for which the current study was underpowered. Certain simplifications of biomechanics were necessary to keep the method practical, but they apply to all patients similarly (blood as noncompressible fluid with constant density, determination of average aortic diameter by a limited number of measurements, aortic length as a function of body height). Limited echo windows may put an obstacle to measurement of aortic diameters; in our case, with experienced echocardiographers using modern equipment with harmonic imaging, this was only a problem in 1% to 2% of patients; at least two aortic diameters were available in all patients. Aortic plaques may have a complex three-dimensional morphology, limiting the accuracy of plaque volume determinations, but because these complex plaques usually occur only with very severe atherosclerosis, we do not believe that this problem led to frank misclassification of our patients.

Clinical implications. Improved noninvasive assessment of global cardiovascular risk is valuable in many situations. In the first line, it may be used in a patient population similar to the one reported, i.e., in patients referred for noninvasive cardiovascular examination, to improve cardiovascular risk estimation and for better selection of high-risk individuals for additional exams and for institution of preventive measures.

Furthermore, individualized risk assessment may also be important for asymptomatic individuals with multiple risk factors or occupational risks, such as pilots. In these, recommendations for lifestyle changes may be better justified and possibly more convincing if atherosclerosis is documented objectively. Lastly, this method might improve patient selection for "primary" prevention of atherosclerosis (e.g., by pharmacologic lipid lowering) to those with objectively documented but clinically silent atherosclerosis, eliminating all patients with risk factors but no echocardiographic evidence of atherosclerosis, with a favorable impact on cost effectiveness in cardiovascular prevention. Noninvasive quantification of atherosclerosis severity will probably enhance, but not replace, conventional risk factor assessment, as these analyses offer complementary information.

We conclude that bedside quantification of atherosclerosis severity is feasible by echocardiographic determination of specific aortic elastance and is strongly associated with the risk of future complications of atherosclerosis beyond conventional risk factors. It therefore promises better cardiovascular risk stratification and improved targeting of "primary" and secondary prevention.

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REFERENCES

1. Scandinavian Simvastatin Survival Study Group. Randomised trial of cholesterol lowering in 4444 patients with coronary heart disease: the Scandinavian Simvastatin Survival Study. Lancet 1994;344:1383–9.
2. Sheperd J, Cobbe S, Ford I, et al. Prevention of coronary heart disease with pravastatin in men with hypercholesterolemia. N Engl J Med 1995;333:1301–7.
3. Fung YC. Mechanical properties of blood vessels. In: Fung YC, editor. Biomechanics: Mechanical Properties of Living Tissues. 2nd ed. New York, NY: Springer, 1993:342.
4. Fung YC. The flow properties of blood. In: Fung YC, editor. Biomechanics: Mechanical Properties of Living Tissues. 2nd ed. New York, NY: Springer, 1993:66.
5. Lang RM, Cholley BP, Korcarz C, et al. Measurement of regional elastic properties of the human aorta: A new application of transesophageal echocardiography with automated border detection and calibrated subclavian pulse tracings. Circulation 1994;90:187–92.
6. Adams JN, Brooks M, Redpath TW, et al. Aortic distensibility and stiffness index measured by magnetic resonance imaging in patients with Marfan's syndrome. Br Heart J 1995;73:265–9.
7. Wright JS, Cruickshank JK, Kontis S, et al. Aortic compliance measured by noninvasive Doppler ultrasound: description of a method and its reproducibility. Clin Sci (Colch) 1990;78:463–8.
8. Anderson KM, Odell PM, Wilson PW, et al. Cardiovascular disease risk profiles. Am Heart J 1991;121:293–8.
9. Blood Vessels. In: Cotran RS, Kumar V, Robbins SL, editors. Robbins Pathologic Basis of Disease. 4th ed. Philadelphia, PA: Saunders, 1989:556.
10. Langewouters GJ, Wesseling KH, Goedhard WJ. The pressure dependent dynamic elasticity of 35 thoracic and 16 abdominal human aortas in vitro described by a five component model. J Biomech 1985;18:613–20.
11. Tanaka TT, Fung YC. Elastic and inelastic properties of the canine aorta and their variation along the aortic tree. J Biomech 1994;7:357–70.
12. Wuyts FL, Vanhuzse VJ, Langewouters GJ, et al. Elastic properties of human aortas in relation to age and atherosclerosis. Phys Med Biol 1995;40:1577–90.
13. Langewouters GJ, Wesseling KH, Goedhard WJ. The static elastic properties of 45 human thoracic and 20 abdominal aortas in vitro. J Biomech 1984;17:425–35; calculation of specific elastance E×h based on reported raw data.
14. London GM, Panner B, Guerin AP, et al. Cardiac hypertrophy, aortic compliance, peripheral resistance, and wave reflection in end-stage renal disease. Comparative effects of ACE inhibition and calcium channel blockade. Circulation 1994;90:2786–96.
15. Cholley BP, Shroff SG, Korcarz C, et al. Aortic elastic properties with transesophageal echocardiography with automated border detection: validation according to regional differences between proximal and distal descending aorta. J Am Soc Echocardiogr 1996;9:539–48.
16. Breithaupt K, Belz GG, Sinn W. Non-invasive assessments of compliance of the aortic wind-kessel in man derived from pulse pressure/storage volume ratio and from pulse wave velocity. Clin Physiol Biochem 1992;9:18–25.
17. Groenink M, de Roos A, Mulder BJ, et al. Changes in aortic distensibility and pulse wave velocity assessed with magnetic resonance imaging following beta-blocker therapy in the Marfan Syndrome. Am J Cardiol 1998;82:203–8.
18. Lehmann ED, Parker JR, Hopkins KD, et al. Validation and reproducibility of pressure-corrected aortic distensibility measurements using pulse-wave-velocity Doppler ultrasound. J Biomed Eng 1993;15:221–6.
19. Lehmann ED, Hopkins KD, Rawesh A, et al. Relation between number of cardiovascular risk factors/events and noninvasive Doppler ultrasound assessments of aortic compliance. Hypertension 1998;32:565–9.
20. Blacher J, Guerin AP, Pannier B, et al. Impact of aortic stiffness on survival in end-stage renal disease. Circulation 1999;99:2434–9.